Dissimilar Allergic Disease in Identical Twins

A Study of Psychosomatic Aspects

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• Identical twins with bronchial asthma were studied. One had the first attack of the disease in late adolescence, the other not until he was adult.

Both were demonstrated by immunologic means to be sensitive to house dust and certain foods. Yet, of itself, the factor of exposure to a known allergen seemed not enough to precipitate clinical allergic reaction in either of them.

It is believed that emotional stress is accompanied by physiologic changes which facilitate increased reactions to antigenic agents that in normal circumstances would not cause clinical disease.

The twins were widely different with regard to emotional development and in their reaction to situations of stress. In both of them allergic manifestations were associated with periods of emotional conflict.

The dissimilar clinical manifestations of allergy in these identical twins may be explained by differences in personality and therefore in reactions to stress situations.

THE CLINICAL SYNDROME of bronchial asthma is the result of pathophysiologic disturbances in the bronchopulmonary system—edema, hypersecretion, and constriction of smooth muscle. The major etiologic factor is assumed to be an antigen-antibody response; that is, a sensitive subject is exposed to an antigenic material and the lungs are the site of an allergic reaction. The cause-effect relationship is not always so clear-cut in individual patients. Exposure to a known antigen may result in clinical asthma under one set of circumstances, but not under another. It may be impossible to link clinical asthma with seasonal incidence of pollen, ingestion of certain foods, or a particular place of residence. Consequently, in recent years many workers have sought to elucidate other factors which, in a susceptible person and in certain circumstances, might combine to produce the clinical syndrome of asthma.

Emotional stress is one such factor which, in combination with a physiologic predisposition, may precipitate an allergic reaction. This association of emotional stress and precipitation of allergic reaction has been demonstrated in the laboratory by Holmes,[10, 11, 12] Wolf and co-workers,[19] Graham,[8] and Treuting[18] and has been commented on by many clinical observers.[1, 3, 5, 7, 13, 15] It should be emphasized, however, that emotional stress *per se* is not the sole causative agent; it is only one of many trigger mechanisms which may set off an allergic reaction in a predisposed person.

Allergic diathesis is thought to be genetically determined. The distribution of genetic predisposition throughout the population, like that of other biologic phenomena, probably occurs in a "bell-shaped" curve, with persons who have a great predisposition to allergic reaction under the slightest stress at one end of the curve and persons who will probably never have allergic disease at the other. Predisposition cannot be measured; development of clinical allergic disease is the only conclusive evidence of its existence. For example, many persons in whom there is no clinical evidence of allergy have positive reaction to skin tests.[14] It may be postulated that later, under the proper circumstances, allergic disease might develop in them.[1] It has been observed that persons with a family history of frequent, severe allergic disease (strong genetic predisposition) tend to have clinical manifestation of allergy early in life. Apparently a specific sensitivity is not inherited, since the presence of circulating antibodies in newborn infants has never been conclusively demonstrated.[2]

The study of clinical evidence of allergy in identical twins should be of interest, since such twins have identical genetic endowments. There have been few such studies, owing to the difficulty of collecting the necessary clinical data.[4, 17] As a matter of fact, the entire problem of genetic transmission in allergic susceptibility is not well defined.[16] If identical twins have clinical manifestations of allergy which differ in time of onset, severity, and reaction pattern, it may be assumed that, since their genetic pattern is

From the Psychosomatic and Allergy Clinics of the Division of Medicine, University of California School of Medicine, San Francisco.

Presented before the Section on Allergy at the 81st Annual Session of the California Medical Association, Los Angeles, April 27-30, 1952.

identical, other factors must modify the organism's response.

It is probable that emotional stress is one of the many factors which modify the organism's response and cause the differences between clinical manifestations in identical twins.

The authors have had opportunity to study a pair of young male twins, A and B, who fulfill the inferential criteria of identity. Unfortunately, complete proof is lacking; the twins were born at home and the placenta was not examined at the time of birth.

A and B are 26 years of age. A has had perennial allergic rhinitis since early childhood and intermittent bronchial asthma since the age of 17 years. B has had sporadic allergic rhinitis since the age of 9 years and intermittent bronchial asthma since he was 24 years old.

The following members of the family are known to have had asthma: Paternal grandmother and her family, maternal aunt, maternal grandfather, and the two-year-old daughter of B. The three-year-old son of A has mild atopic eczema.

A had a short episode of "croup" at the age of 6 years; B had one episode of hives at the age of 5 or 6 years and "chest trouble" for several months at the age of 9 years. A has had perennial allergic rhinitis since early childhood; in B's case, allergic rhinitis began later and has not been as frequent or severe. A had edema and itching of the eyes, following a first and only injection of penicillin when he was 21 years old. A has also had several episodes of conjunctivitis since the age of 21 years. A had edema of the lips after eating crab at the age of 25 years. Subsequently, he ate crab, but had no allergic reactions. B had conjunctivitis, which was diagnosed as chronic non-specific keratoconjunctivitis and which responded to local application of cortisone, when he was 26 years old. Both twins have had frequent canker sores since childhood.

On physical examination, A was found to be slightly heavier than B. The nasal mucosa of both twins was slightly edematous and pale, and a thin watery discharge was apparent. Upon examination of the lungs of both patients, musical rhonchi and expiratory wheezing were heard. Early emphysematous changes were noted in A.

Numerous eosinophils were observed in stained specimens of nasal and bronchial secretions from each twin.

Both A and B had strong positive reactions to scratch tests with house dust. Neither had reactions to either scratch or intradermal tests with other miscellaneous inhalants, and there was no reaction to scratch tests with various pollens of trees, grasses and weeds. A had positive reactions to scratch tests with fresh frozen crab and shrimp, as well as to extracts of crab and shrimp, but results of all other scratch and intradermal tests with foods were negative. B had positive reactions to scratch tests with fresh frozen chicken, anchovy, cod, and sole; but he did not have reactions to scratch and intradermal tests with extracts of these and other foods.

Factors indicating the subjects were identical twins were:

1. The blood groups were identical: O. Rh_0, Rh_1, Rh″, Hr′, Hr″, and MN positive.

2. Great similarity in bony structure, including dentition, as determined by x-ray examination.

3. Somatotyping performed by an independent observer strongly supported true identity.

4. Fingerprints were compatible with identity.

Both parents and one older sister, aged 37 years, are living. The father has had myocardial infarction and has occlusive vascular disease. The sister has diabetes.

The father is a successful businessman, active and extroverted, who drinks and smokes heavily. He was described by the twins as a "good guy, but with little time for the family." The mother has a rather dominant personality, is of rigid demeanor, has a strict religious and moral code, is demanding of husband and children, stressing obedience, and has a great desire to achieve social and financial standing. Despite long-standing marital discord, there has been no formal separation, since both parents are satisfied to go their separate ways. The twins respect and admire their sister, although because of the difference in ages their relationship with her is not close.

A is 15 minutes older than B, and both twins have always felt A was the parents' favorite. A admires and respects his father, wants to please and emulate him but has been somewhat passive in their relationships. The father treats A as though he were still a young boy. Although A respects his mother he has never felt the same affection toward her that he feels toward his father.

B apparently likes his father, but is no more than tolerant of what he regards as his father's weaknesses (for example, "little time for the family"). It is B's opinion that his parents' success is owing to the mother's domination, perseverance and drive. He also said that his mother is the stronger person. As a child, although he resented her demands and his need to comply with her wishes, he felt closer to her than to his father. He finds difficulty, however, in verbally expressing any feeling of true affection for her. It appears that B has always felt rejected by both parents and has reacted with hostility and strong efforts to gain independence. He feels that his mother made more demands on him than on A and that A in some way could "get around" her.

As children, the twins were both aware of their

rivalry. A was always a little larger physically and more popular in school, but B was the better athlete and a better student. A believes he had more natural athletic ability but did not try as hard as B did. During their senior year in high school when they were 17 years old, A had his first attack of asthma, which lasted three months. At the time he was temporarily away from home and working part-time.

After finishing high school, the twins joined different branches of the armed services. A had no attacks of asthma (allergic rhinitis?) while in the service and felt he was successful in his service career. Apparently he liked the idea of separation from his parents. While A was in the service, he married a girl two years older than he. The marriage has been happy. The couple has two sons, 6 and 3 years old. The youngest has very mild atopic eczema.

B did not like the service and was rather unhappy, but had good health. Soon after he was discharged, B married a girl three years younger than he. They have three daughters, aged 4, 2, and 1 year. The two-year-old daughter has had several attacks of wheezing respiration. B's wife is not of his religious faith, which apparently was and is disturbing to his mother. B and his wife disagree about religion and the religious education of the children. In religion, as in other areas, B has a rather intellectualized approach and has "his own concepts of religion." Apparently B does not like his wife's parents and prefers to have little contact with them. In spite of these problems, the marriage seems stable.

After being discharged from the service at the age of 20 years, A returned to school and was free of asthma until a severe attack developed the week before final examinations and persisted until a week after examinations. He began professional school one year later, and again asthmatic attacks occurred before and continued through examinations. He withdrew from school for one year because of asthma and conjunctivitis. During that year, he was free of asthma, although he lived in the same home. Upon resuming schooling, he had asthma before and during every final examination. Yet he had an admirable academic record. Since he has been practicing his profession, he has had attacks during periods when he was under pressure to "produce and succeed." A believes that tenseness, nervousness, and being under pressure are the major precipitating factors.

B also reentered college after being discharged from the service and at about the time of his marriage. He floundered for two or three years, not knowing what career to pursue. He tended to follow the lead of A in choosing a course of study and finally decided to follow the same profession. At the age of 24 years, he entered professional school and moved to a new locality. One year later, after he had lived in the new locality for eight or more months, he moved to a new home in the same town. Soon afterward he had his first attack of asthma. Subsequently he moved to another house in the same block, but asthmatic attacks persisted. The following summer he worked in an area about 25 miles from his home and returned home every night. During this period he was free of asthma. B's attacks of asthma apparently have never been as severe as A's and are not precipitated by the stress of examinations. B associates attacks with feelings of guilt about not working or studying. He has a need to work hard and is reluctant to accept help from his family.

In summary, A has a great need to succeed in order to please other people. His whole life is directed toward achieving success so that he will be acclaimed by his family and friends. Every move seems to be calculated on the basis of what people will think about him. It may be that he is continually striving to maintain his favored position in reference to his twin brother. In any event, his overt personality is such that he is socially acceptable; he is pleasant, ingratiating, and makes an effort to have people like him. It is obvious, however, that when he is faced with a situation in which he must prove his ability to others — in tests, for example — the tension is so great that it precipitates an attack of asthma.

On the other hand, B seems to have a different attitude. It appears that he responded to A's favored position and his mother's demands by reacting with open hostility and denial of dependence. However, there is some identification with the mother, in that he is compulsive and rigid in his beliefs. In adult life he has tended to intellectualize all his problems and to distrust emotions. Once he is certain of the correctness of his ideas, he is willing to argue with anyone. He may even go out of his way to provoke an intellectual debate, thus providing a release for hostility. He is conscious of his rivalry with A and is continually trying to outdo him. Because of his somewhat rigid and combative exterior, he is not as socially acceptable as A and, it seems probable, not as well liked. Since his asthma was later in onset and not as severe, however, it may be assumed that he is more effective in handling his inner tensions.

Thorough psychological testing of the twins has been carried out by an independent observer. It is of interest that their intelligence quotient scores were very close. In general, the psychologist's impression coincided with the clinical formulation.

Because of the family history, it is assumed that these twins have a strong genetic allergic diathesis. Consequently their tissues respond to certain stimuli by the development of edema, hypersecretion, and smooth muscle spasm—that is, clinical allergic disease. The twins were demonstrated to have immuno-

logic allergy—the capacity to react to certain agents —as well as clinical allergic disease. However, it is known that clinical allergic disease may occur in the absence of demonstrable immunologic allergy—that is, factors other than antigen-antibody reactions may produce the pathophysiologic response defined as clinical allergic disease.[8-12, 13, 19] It has been shown that emotional stress may be accompanied by vascular changes that are identical with those seen in immunologic allergy.[8-12, 19] These vascular changes, namely, decreased constrictor tone of arterioles and capillaries, accompanied by increased permeability, are thought to be due to the liberation of acetylcholine at vasomotor nerve endings. Holmes[10] demonstrated that such vascular phenomena can be produced in the nose, following interruption of sympathetic vasoconstrictor nerves by injection of procaine into the stellate ganglion.

It is probable that both immunologic allergy and non-allergic vascular phenomena are of importance in producing clinical allergic reactions in a given person. At one time the immunologic phase may predominate, while at another time non-allergic vascular reactions may be of primary importance. Holmes[10] reported that the severity of clinical allergic response following exposure to an antigen may be greatly modified by the preexisting vascular status of the tissues involved. This may be the physiologic explanation for the clinical observation that a given subject may have clinical allergic response on exposure to a known antigen under one set of circumstances, and at other times have no clinical response to the same antigen. The thesis that changes in autonomic innervation may modify allergic phenomena is supported by the observation of Funkenstein[6] that variations in an individual's physiologic responses to injected acetylcholine and epinephrine are related to activity or remission of clinical allergic disease.

The twins reported upon here, in whom the genetic background is identical, are strikingly different with regard to allergic manifestations. The age at onset was not the same and there was no similarity in the pattern of attacks. Both were demonstrated by immunologic means to be sensitive to house dust and certain foods. There was no clinical evidence to suggest that food was an important antigenic agent in the development of rhinitis and asthma in these patients. It can be assumed, however, that exposure to house dust was important. The exposure of the twins to house dust was relatively constant, although the clinical manifestation of allergy, especially in the case of A, usually occurred in connection with particular types of stress. The authors believe that emotional stress is accompanied by certain physiologic changes which precipitate clinical allergic disease, and that in the twins herein reported upon both immunologic allergy and the pathophysiologic vascular changes accompanying emotional stress are of importance in the genesis of clinical allergic reactions.

The differences in the types of situation that produce emotional stress in these twins may be understood in the light of their personality development. The overt stress-producing situations are more clearly defined in A than in B and can be more clearly correlated with the development of episodes of clinical allergic disease. It is of interest that although A is on the surface a better adjusted individual, the price of this adjustment is more frequent emotional tension which is reflected by an increased incidence of clinical allergic manifestation.

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